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EXAMINER	
SHIN, DANA H	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/588,602	TANG ET AL.	
	Examiner	Art Unit	
	DANA SHIN	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 April 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,23,28 and 48-67* is/are pending in the application.

4a) Of the above claim(s) *23,28 and 65-67* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 48-64* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 August 2006* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8-5-2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Notice to Comply*

DETAILED ACTION

Election/Restrictions

Applicant's election of claims 1-6, 8-11, 13-14, 16-19, and 21-22 in the reply filed on April 20, 2010 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Status of Claims

Claims 1, 23, 28, and 48-67 are currently pending in the instant application. Claims 23, 28, and 65-67 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Accordingly, claims 1 and 48-64 are under examination on the merits in the instant case.

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. See pages 44-45. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Drawings

The drawings in Figures 2, 6B, 7B, 9, 10, 11, and 12 are objected to under 37 CFR 1.83(a) because they fail to show the expression patterns as described in the specification. Applicant is advised to adjust the brightness/darkness and/or contrast levels of the drawings to clearly show the microscopic, anatomical, and Western blot results. Any structural detail that is essential for a proper understanding of the disclosed invention should be shown in the drawing. MPEP § 608.02(d). Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Specification

The disclosure is objected to for containing sequence rule non-complaint subject matter. See pages 46-62, which contain nucleotide sequences that are at least 10 nucleotides in length but are not accompanied by appropriate SEQ ID NOs. See also the attached Notice to Comply.

Appropriate correction is required.

Priority

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 60/541,775, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. It is found that the disclosure of 60/541,775 is completely silent about the claimed subject matter, which is an oligonucleotide targeted to Bcl-2 A1. It is noted that 60/541,775 fails to provide adequate support for the instantly claimed target

gene, Bcl-2 A1, let alone the claimed SEQ ID NO:291. Accordingly, the benefit of the 60/541,775 filing date for claims 1 and 48-64 is denied, and therefore the filing date of PCT/US05/0357, which is February 7, 2005, will be the effective filing date for claims 1 and 48-64.

If applicant believes that the claimed subject matter is adequately supported by the disclosure of 60/541,775, applicant is advised to point out the particulars in response to this Office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 50-51 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 50-51 recite the limitation "wherein the one or more additional double-stranded oligonucleotides" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim. Note that claim 49 recites only "one or more additional dsRNA oliognucleotides".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 52-53, and 55-56 are rejected under 35 U.S.C. 102(b) as being anticipated by Drumm et al. (WO 03/087368 A2).

Drumm et al. teach that a dsRNA targeted to BCL2A1 is useful for treating disorders related to the eye (e.g., age-related macular degeneration, choroidal neovascularization, retinal neovascularization, retinal blastoma, retinal astrocytoma) when the dsRNA further comprising a pharmaceutically acceptable carrier is introduced to the eye and inhibits BCL2A1 expression in the eye. They teach that the dsRNA molecules can be delivered via therapeutic gene delivery vectors or polyethylene glycol (PEG) or liposomes. See pages 3, 6-12, 20-21, 28-29, 39-40, 52-53, 56; claims 49-50 and 90. Accordingly, all claim limitations are taught by Drumm et al.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1 and 48-64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Drumm et al. (WO 03/087368 A2) in view of PR Newswire (Studies Demonstrate Potential Clinical Utility of siRNA in Ophthalmic Disease, May 5, 2003, New York) and Reich et al. (US 2004/0180357 A1).

Drumm et al. teach that a dsRNA targeted to BCL2A1 (NM_004049) is useful for treating disorders related to the eye (e.g., age-related macular degeneration, choroidal neovascularization, retinal neovascularization, retinal blastoma, retinal astrocytoma) when the dsRNA further comprising a pharmaceutically acceptable carrier is introduced to the eye and inhibits BCL2A1 expression in the eye. They teach that the dsRNA molecules can further comprise 3'-dTdT overhang sequences on the sense and antisense strands. They teach that the dsRNA molecules can be delivered via therapeutic gene delivery vectors or polyethylene glycol (PEG). See pages 3, 6-12, 20-21, 28-29, 39-40, 52-53, 56; claims 49-50 and 90. Drumm et al. do not teach that the anti-BCL2A1 dsRNA is targeted to the nucleotide sequence of "AACCTGGATCAGGTCCAAGCA" of NM_004049.

The article published in PR Newswire teaches an siRNA-based pharmaceutical composition and a method of reducing VEGF activity by delivering the siRNA-based composition into the mouse retina *in vivo*. The article teaches that the siRNA composition targeting VEGF is expected to be marketed for treatments for wet age-related macular degeneration (ARMD) and diabetic retinopathy by Acuity Pharmaceuticals and that the market for these ophthalmic diseases is anticipated to grow to $10 billion by 2010.

Reich et al. teach that siRNAs targeted to ocular neovascularization-related genes such as VEGF and HIF-1 alpha are useful for treating ocular neovascularization-related diseases such as ARMD, wherein HIF-1 alpha is a transcriptional regulator of VEGF. They teach that siRNAs designed to target the 5'-AA(N19) sequence motif are effective in reducing target expression as they experimentally demonstrate that an siRNA targeted to the 5'-AA(N19) sequence motif of HIF-a alpha (see SEQ ID NO:297) reduces HIF-1 alpha as well as VEGF expression levels in the eye of a subject and reduces ocular angiogenesis in the subject with a statistical significance, wherein the siRNA (see SEQ ID NOs:298 and 299) comprises a 3'-TT overhang sequence at the 3' end of the sense strand (SEQ ID NO:298) and the antisense strand (SEQ ID NO:299). They teach that a combination of different siRNAs targeted to different genes can be administered to treat ocular angiogenesis, wherein the siRNAs comprise a vector or polycations or a hydrophilic polymer or a ligand molecule that can target vascular endothelial cells near the site of angiogenesis. See paragraphs 0010-0014, 0036-0037, 0071, 0079, 0081-0091, 0114-0120; Figure 3.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make an siRNA molecule targeted to the 5'-AA(N19) sequence motif of BCL2A1 (NM_004049) and formulate the siRNA molecule as a pharmaceutical composition for ocular neovascularization-related disease treatment.

One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success so as to make a pharmaceutically useful siRNA agent for ocular neovascularization-related diseases such as age-related macular degeneration, because inhibiting BCL2A1 with a double-stranded RNA targeted to BCL2A1 was taught to be useful for treating

ophthalmic disorders including ARMD as taught by Drumm et al., and because the methodologies and techniques for making target-specific therapeutic siRNA molecules, formulating pharmaceutically suitable siRNA-based ophthalmic compositions, and delivering the siRNA molecules for ocular disease treatment methods were known and were within the technical grasp of one of ordinary skill in the art as taught by the cited prior art references. In particular, the prospect of financial gains by marketing siRNA-based ophthalmic pharmaceutical compositions was expected to be profitable as reported by the Newswire article. As such, one of ordinary skill in the art would have been further motivated to make and market an therapeutically useful siRNA composition targeted to BCL2A1, which is taught to be useful for treating age-related macular degeneration, choroidal neovascularization, retinal neovascularization, retinal blastoma, retinal astrocytoma by Drumm et al. In addition to the usefulness of an siRNA compound targeted to BCL2A1 and the potential marketability of such compound, the prior art also taught how to select effective siRNA sequences as taught and experimentally shown by Reich et al. As such, given the successful inhibition of ocular angiogenesis in a subject with an siRNA designed and selected based on the "5'-AA(N19)" sequence motif rule as shown by Reich et al., when searching for the "5'-AA(N19)" sequence motif within the coding region of the target sequence of NM_004049 (see the attached GenBank citation), one of ordinary skill in the art would have reasonably identified the "AA(N19)" sequence motif located at nucleotides 257-277, wherein the sequence motif corresponds to the nucleotide sequence of SEQ ID NO:219 claimed in the instant case.

Further, it would have been obvious to make a combination composition comprising two or more different siRNAs targeted to different or same angiogenesis-related genes because Reich

et al. taught that one or more siRNA molecules targeted to different target genes can be used to treat angiogenic-related diseases. In fact, even without the explicit teaching of Reich et al. that one or more siRNA molecules targeted to different target genes can be used to treat angiogenic-related diseases, it would have been *prima facie* obvious to make a combination composition comprising two different anti-BCL2A1 dsRNAs or the anti-BCL2A1 comprising SEQ ID NO:219 and the VEGF-A siRNA of Acuity Pharmaceuticals or the HIF-1A siRNA of Reich et al. for greater or enhanced therapeutic effects for age-related macular degeneration or diabetic retinopathy, wherein both anti-BCL2A1 siRNA and anti-VEGF signaling pathway siRNAs are known to be useful to treat ocular neovascularization-related diseases such as age-related macular degeneration or diabetic retinopathy. See *In re Kerkhoven* 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980), wherein the court expressed the following: "It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose…[T]he idea of combining them flows logically from their having been individually taught in the prior art."

In view of the foregoing, the claimed invention taken as a whole would have been *prima facie* obvious at the time of filing.

Claims 1 and 48-64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Drumm et al. (WO 03/087368 A2) in view of Kim et al. (*The American Journal of Pathology,* 2004, 165:2177-2185).

Drumm et al. teach that a dsRNA targeted to BCL2A1 (NM_004049) is useful for treating disorders related to the eye (e.g., age-related macular degeneration, choroidal

neovascularization, retinal neovascularization, retinal blastoma, retinal astrocytoma) when the dsRNA further comprising a pharmaceutically acceptable carrier is introduced to the eye and inhibits BCL2A1 expression in the eye. They teach that the dsRNA molecules can further comprise 3'-dTdT overhang sequences on the sense and antisense strands. They teach that the dsRNA molecules can be delivered via therapeutic gene delivery vectors or polyethylene glycol (PEG). See pages 3, 6-12, 20-21, 28-29, 39-40, 52-53, 56; claims 49-50 and 90. Drumm et al. do not teach that the anti-BCL2A1 dsRNA is targeted to the nucleotide sequence of "AACCTGGATCAGGTCCAAGCA" of NM_004049.

Kim et al. teach that siRNAs targeted to VEGFA, VEGFR1, and VEGFR2 designed by following the Tuschl siRNA design rules are effective in inhibiting ocular angiogenesis when the siRNAs are delivered via peptide (RGD) conjugation to the eye of a mouse. They teach that all of the target sequences for VEGFA, VEGFR1, and VEGFR2 siRNAs have the 5'-AA(N19) sequence motif and that the sense and antisense strand sequences are each 21-nucleotide long with a two TT overhang sequence at the 3' end. See the Materials and Methods at page 2178. They experimentally show that the siRNAs having the 5'-AA(N19) followed by the TT 3' overhang sequence are very effective in reducing the respective target expression levels in the eye and reducing ocular angiogenesis when the mix of all three siRNAs targeting the VEGF pathway is delivered to the eye in a polymer-based delivery vehicle comprising PEG and arginine-glycine-aspartate (RGD) peptide. They teach that VEGF signaling pathway-targeting siRNAs are therapeutically useful for treating neovascularization-related eye diseases such as stromal keratitis, diabetic retinopathy, and age-related macular degeneration. See the entire reference.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a combination composition comprising an siRNA molecule targeted to the 5'-AA(N19) sequence motif of BCL2A1 (NM_004049) and one or more VEGF signaling pathway-targeting siRNA molecules of Kim et al.

One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success so as to use the combination product for inhibiting ocular angiogenesis, thereby treating stromal keratitis, diabetic retinopathy, and age-related macular degeneration, because a dsRNA targeted to BCL2A1 was taught to be useful for inhibiting ocular angiogenesis and thus treating ocular neovascularization-related diseases as taught by Drumm et al., and because a combination of three siRNAs targeted to VEGFA, VEGFR1, and VEGFR2 was shown to be effective in reducing ocular angiogenesis and thus suggested to be useful for treating ocular neovascularization-related diseases as taught by Kim et al. Since Kim et al. experimentally demonstrated the efficacy of siRNAs designed to target the 5'-AA(N19) sequence motif within the given target sequence, when searching for the "5'-AA(N19)" sequence motif within the coding region of the target sequence of NM_004049 (see the attached GenBank citation), one of ordinary skill in the art would have reasonably identified the "AA(N19)" sequence motif located at nucleotides 257-277, wherein the sequence motif corresponds to the nucleotide sequence of SEQ ID NO:219 claimed in the instant case.

Further, it would have been *prima facie* obvious to make a combination composition comprising two different anti-BCL2A1 dsRNAs or the anti-BCL2A1 comprising SEQ ID NO:219 and the VEGF-A siRNA or VEGF-R1 siRNA or VEGF-R2 siRNA of Kim et al. for greater or enhanced therapeutic effects for age-related macular degeneration or diabetic

retinopathy, wherein both anti-BCL2A1 siRNA and anti-VEGF signaling pathway siRNAs are known to be useful to treat ocular neovascularization-related diseases such as age-related macular degeneration or diabetic retinopathy. See *In re Kerkhoven* 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980), wherein the court expressed the following: "It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose…[T]he idea of combining them flows logically from their having been individually taught in the prior art."

Since all skills, knowledge, and information required to arrive at the claimed invention were known and within the ordinary capabilities and technical grasp of one of ordinary skill in the art, the claimed invention taken as a whole would have been *prima facie* obvious at the time of filing.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225

USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 50-51 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 19 of U.S. Patent issuing from claim 85 of Application No. 10/551,667 in view of Drumm et al. (WO 03/087368 A2).

Although the conflicting claims are not identical, they are not patentably distinct from each other because both the instant claim and the reference claim are drawn to a double-stranded RNA composition comprising an siRNA targeted to EGFR-RP. Note that the transitional term "comprising" is open-ended and does not exclude any unrecited elements. With regard to the claimed double-stranded nucleic acid molecule of the reference case, the specification of 10/551,667 teaches that an siRNA targeted to EGFR-RP inhibits angiogenesis. Further, it was known in the art that an siRNA targeted to BCL2A1 inhibits angiogenesis as taught by Drumm et al. Hence, it would have been obvious to make a composition comprising an siRNA targeted to

BCL2A1 and an siRNA targeted to EGFR-RP for angiogenesis inhibition in view of *In re Kerkhoven* 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). Hence, the subject matter of claims 50-51 of the instant application is an obvious variant of that of claim 85 of Application No. 10/551,667 that is issuing as claim 19 of U.S. Patent.

Claims 50-51 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 8 of U.S. Patent No. 7,723,316 issuing from claim 46 of Application No. 11/824,426 in view of Drumm et al. (WO 03/087368 A2).

Although the conflicting claims are not identical, they are not patentably distinct from each other because both the instant claim and the reference claim are drawn to a double-stranded RNA composition comprising an siRNA targeted to VEGF-R1 and one or more additional siRNAs that decrease the expression of an angiogenic gene. It was known in the art that an siRNA targeted to BCL2A1 inhibits angiogenesis as taught by Drumm et al. Hence, it would have been obvious to make a combination composition comprising an siRNA targeted to BCL2A1 and an siRNA targeted to VEGR-R1 for angiogenesis inhibition as claimed in the reference claim. Hence, the subject matter of claims 50-51 of the instant application is an obvious variant of that of claim 46 of Application No. 11/824,426 that is issuing as claim 8 of U.S. Patent. No. 7,723,316.

Claims 50-51 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 43 of copending Application No. 11/894,567 in view of Drumm et al. (WO 03/087368 A2).

Although the conflicting claims are not identical, they are not patentably distinct from each other because both the instant claim and the reference claim are drawn to a double-stranded RNA composition comprising an siRNA targeted to VEGFR1 or VEGR2 or VEGFR3. Note that the transitional term "comprising" is open-ended and does not exclude any unrecited elements. It was known in the art that an siRNA targeted to BCL2A1 inhibits angiogenesis as taught by Drumm et al. Hence, it would have been obvious to make a composition comprising an siRNA targeted to BCL2A1 and an siRNA targeted to VEGFR1 or VEGR2 or VEGFR3 for angiogenesis inhibition. Hence, the subject matter of claims 50-51 of the instant application is an obvious variant of that of claim 43 of Application No. 11/894,567.

This is a provisional obviousness-type double patenting rejection.

Claims 50-51 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 2 of copending Application No. 12/682,615 in view of Drumm et al. (WO 03/087368 A2).

Although the conflicting claims are not identical, they are not patentably distinct from each other because both the instant claim and the reference claim are drawn to a double-stranded RNA composition comprising an siRNA targeted to VEGFR1. Note that the transitional term "comprising" is open-ended and does not exclude any unrecited elements. It was known in the art that an siRNA targeted to BCL2A1 inhibits angiogenesis as taught by Drumm et al. Hence, it would have been obvious to make a composition comprising an siRNA targeted to BCL2A1 and an siRNA targeted to VEGFR1 for angiogenesis inhibition in view of *In re Kerkhoven* 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980), which is the subject matter claimed in the instant

case. Hence, the subject matter of claims 50-51 of the instant application is an obvious variant of that of claim 2 of Application No. 12/682,615.

This is a provisional obviousness-type double patenting rejection.

Claim 50 is provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 12 of copending Application No. 12/667,889 in view of Drumm et al. (WO 03/087368 A2).

Although the conflicting claims are not identical, they are not patentably distinct from each other because both the instant claim and the reference claim are drawn to a double-stranded RNA composition comprising one or more siRNAs targeted to angiogenic genes Ang-1, Ang-2, or Tie-2. Note that the transitional term "comprising" is open-ended and does not exclude any unrecited elements. It was known in the art that an siRNA targeted to BCL2A1 inhibits angiogenesis as taught by Drumm et al. Hence, it would have been obvious to make a composition comprising an siRNA targeted to BCL2A1 and an siRNA targeted to Ang-1, Ang-2, or Tie-2 for angiogenesis inhibition. Hence, the subject matter of claim 50 of the instant application is an obvious variant of that of claim 21 of Application No. 12/667,889.

This is a provisional obviousness-type double patenting rejection.

Claim 50 is provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 16 of copending Application No. 12/678,721 in view of Drumm et al. (WO 03/087368 A2).

Although the conflicting claims are not identical, they are not patentably distinct from each other because both the instant claim and the reference claim are drawn to a double-stranded RNA composition comprising one or more siRNAs including an siRNA targeted to HIF-1 alpha. Note that the transitional term "comprising" is open-ended and does not exclude any unrecited elements. It was known in the art that an siRNA targeted to BCL2A1 inhibits angiogenesis as taught by Drumm et al. Hence, it would have been obvious to make a composition comprising an siRNA targeted to BCL2A1 and an siRNA targeted to HIF-1 alpha for angiogenesis inhibition. Hence, the subject matter of claim 50 of the instant application is an obvious variant of that of claim 16 of Application No. 12/678,721.

This is a provisional obviousness-type double patenting rejection.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DANA SHIN whose telephone number is (571)272-8008. The examiner can normally be reached on Monday through Friday, 7am-3:30pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Fereydoun Sajjadi (Acting SPE) can be reached on 571-272-3311. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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